Contribution ID: **14** Type: **not specified**

Targeting the undruggable: preliminary studies on a promising beta-catenin inhibitor

Wednesday, 11 May 2022 10:40 (20 minutes)

The WNT signal transduction cascade is a key regulatory pathway during embryonic development and adult tissue homeostasis. In the canonical WNT pathway, the armadillo repeat protein β-catenin serves as the central signaling molecule by engaging in crucial protein-protein interactions (PPIs) with both positive and negative effectors of the pathway and by linking WNT ligand mediated pathway activation to target gene induction in the nucleus. Aberrant WNT pathway activation, leading to nuclear accumulation of β-catenin, is considered as a key driver event for initiation and progression of many cancers, including colorectal and hepatocellular carcinomas. Despite significant efforts made to identify modulators or inhibitors of WNT pathway, β-catenin is still deemed by most as an "undruggable" target and specific drugs against the signaling pathway for clinical treatment have not been approved yet. Here we present our preliminary data describing a promising interaction between the β-catenin armadillo repeats and the non-peptidic small molecule RS6452. In particular, results obtained by Surface Plasmon Resonance direct binding assay along with the structural investigation of the protein/ligand complex by X-ray crystallography will be presented, highlighting the scientific relevance of this discovery and focusing on the further experimental strategy to assess the potential of RS6452 as new anticancer drug.

Presenter: Dr CAPELLI, Davide (CNR - Istituto di Cristallografia)

Session Classification: Sessione